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Sick Neighborhood Syndrome: Population with Multiple Chemical Sensitivity Adjacent to Bioethanol Distillery

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Abstract

The population of a neighborhood in the city of Córdoba presents general irritant symptoms since a bioethanol distillery began to operate there, from which formaldehyde, toluene, xylene mainly emanate. At the request of the community, collective environmental health was evaluated with a cross-sectional study of prevalence of these conditions. 53% of the residents reported respiratory disorders, conjunctivitis 31%, headaches 27%, dermatitis 23% and dyspepsia 22%. 57% of children aged 6 - 7 use bronchodilators (an indicator of asthma). 66% of the population has one of these conditions, 46% has two and 26% has three; children are the most affected. The results coincide with the Consensus on Multiple Chemical Sensitivity Syndrome in that it is reproducible by repeated chemical exposure, is chronic and does not improve without eliminating exposure, affecting multiple organs and systems. 14.8% of newborns feature malformations, while in the rest of the city, only 1.7% did. Similar to the Sick Building Syndrome, the collective health picture found suggests a "Sick Neighborhood Syndrome".

Keywords

Multiple Chemical Sensitivity, Environmental Exposure, Air Pollution, Environmental Health, Formaldehyde

1. Introduction

The San Antonio neighborhood is located south of the city of Córdoba. Many of its inhabitants feature eye, skin and respiratory irritations, coupled with fatigue and dysphoria. The intensity of these features has been on the rise and some neighbors even had to leave the neighborhood, following doctor's advice. The neighborhood is an over 40-year-old settlement. In February 2012, a bioethanol

distillery [1] started operating there, next to the backyard of family homes, producing 100,000 liters of bioethanol daily. A company called *Porta Hnos.* had been manufacturing liquor and bioethanol since 1995 (**Figure 1**). In 2012, a new structure was set into motion which distills bioethanol through corn grinding and fermentation. In 2013, the Environment and Health University Network (REDUAS, for its Spanish acronym) of the School of Medicine of the National University of Córdoba performed an epidemiological assessment of over 74% of San Antonio residents reporting highly-frequent irritant disorders lead by headaches (43%), followed by eye congestion (34%), respiratory disorders (33%), digestive distress (26%), and irritant dermatitis (18%). [2] In November 2014, courts from the province of Córdoba requested an environmental chemical expert report. Such report confirmed that the plant's fermenters were releasing chemical substances that could explain the symptoms suffered by the neighbors living in that area, mainly toluene, xylene, hexane, acetic acid, ethanol, and others, which, together with formaldehyde, were detected in the air samples taken in the streets of San Antonio [3], apparently at lower levels than those set by exposure guidelines currently in force in Argentina. Ambient air does not normally contain these chemical contaminants, environmental standards guidelines determine minimum values that are estimates of safety, although not certain.

In 2016, San Antonio neighbors requested REDUAS to conduct a new environmental collective health assessment in the neighborhood and also in Residential San Antonio (another neighborhood located 150 meters southeast of San Antonio). The study included here was designed for such assessment in order to evaluate whether the symptoms or medical conditions featured by neighbors constitute a specific nosological entity that could be related to the particular environmental pollution in this area of the city of Córdoba.

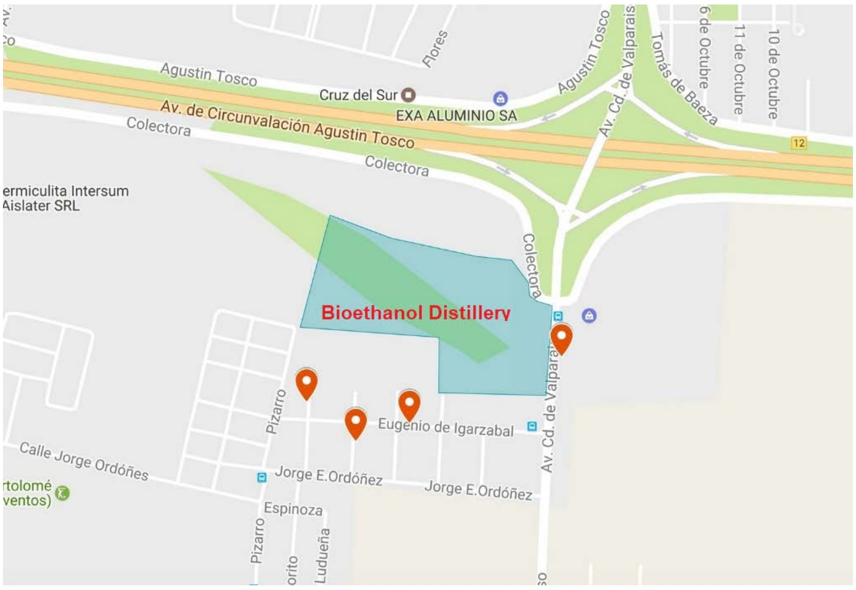


Figure 1. Map of the San Antonio neighborhood and location of Porta Hnos. Bioethanol Plant.

2. Material and Methods

A descriptive, cross-section study was performed to measure the incidences and prevalences of the different clinical features, through a survey targeted to all residents of the San Antonio and Residential San Antonio neighborhoods of the city of Córdoba (population survey). To that end, all houses within the area were visited considering the neighborhood as a single population set, assuming a common, non-differentiated environmental exposure risk. Based on the geographical, demographical and sociological information on the neighborhood from secondary sources, the community under study was accurately characterized and probable environmental pollution causes present in the area were sought. To identify sanitary problems within the community, qualitative techniques were applied through interviews with key informants—such as primary care doctors and nurses in the area, social prominent figures of the neighborhood, school teachers and engineers working at the factory.

The analysis considered variables dependent on: 1) recurrent or allergic irritant dermatitis; 2) recurrent irritant and/or congestive airway disorders and asthma (in this case, the criterion was regular use of bronchodilator aerosol inhalers); 3) persistent headaches or headaches present for 15 or more days a month [4]; 4) digestive disorders, such as gastritis and chronic dyspepsia; 4) chronic or recurrent conjunctivitis or pink eye syndrome; 5) children born with congenital anomalies in the last 5 years; 6) miscarriages in the past 5 years; 7) cancer in any location diagnosed within the last 12 months (incidence); 8) cancer diagnosis in the past 5 years—resident being alive when survey was conducted (prevalence)—and 9) cancer mortality in the past 5 years, following Globocan-IARC criteria [5]. Independent variables were age, sex, and seniority in the neighborhood. Confusion variables included toxic habits (smoking and alcoholism), and occupation. A database was created, as well as a numeric matrix. The prevalence of each disorder was confronted with the reference rates informed by local, national or international official and/or academic entities. Finally, a Pearson correlation analysis was performed on the variables in search of significant associations, which were also measured with contingency tables. For such purposes, the following programs were used: Excel, INFOSTAT, Minitab 17, and EPIDAT.

A questionnaire previously validated by *REDUAS* was used. Most questions were closed while the two final ones were open. All interviews were conducted by medical professionals or senior students in the last year of Medicine at the University of Córdoba (UNC). The entire research was performed under Article 2 of Provincial Law No. 9694 of the Province of Córdoba which governs observational studies on human health [6]. An informed prior consent was requested and recorded for all interviews.

3. Results

Field work was carried out in October 2016. Information was gathered from 134

households (123 in Residential San Antonio and 11 in San Antonio), reaching 65% of the total population, based on the 2008 provincial census. 508 people were examined, out of which 256 were women (50.39%), with a prevalence of young and adult people (Table 1). The average time of residence in the area was 17.11 years.

From an economic standpoint, the neighborhood featured a number of small shops and some warehouses with several workshops. Most neighbors were teachers and workers (very few were hired by the bioethanol distillery of Porta Hnos.) and there were some professionals and businessmen. Unemployment reaches 1.5% of the population.

The pollution sources observed in the area included a mobile antenna, sewage waste in some streets, two small metallurgic workshops, a lumber yard, and the corn-fermenting bioethanol chemical plant. There are no high-voltage lines crossing the neighborhood or high-to-medium voltage electric power transformers creating electromagnetic radiation.

Pathologies Found: Respiratory disorders featured a 53% rate (267/508), asthma (people using bronchodilator inhalers) is suffered by 17% (85/508) of neighbors—climbing to 29% in children under 15 years of age and to 57% in children between 6 and 7 years of age, which are the global epidemiological control group for this disorder [7]—conjunctivitis is suffered by 31% (158/508) of residents, headaches by 27% (135/508), dermatitis by 23% (116/508), and digestive distress by 22% (112/508).

In the past year, seven babies were born, two of them with congenital anomalies (28.6% rate.) Since the start of operations by the bioethanol distillery in the area (5 years), twenty-seven children have been born (2016 birth rate of 13.8/1000 residents,) four of whom showed significant anomalies (14.5% birth defects rate).

Table 1. Population structure of San Antonio and residential San Antonio neighborhoods by sex and age.

Population Feature	Number	Percentage
Total Population	508	100%
Women	256	50.39%
Men	252	49.61%
Children aged 0 - 15	120	23.62%
Youngsters aged 16 - 30	126	24.80%
Adults aged 31 - 50 years	116	22.83%
Adults aged 51 - 65 years	92	18.11%
Adults older than 66	47	9.25%
No data	7	
Age Mean	34.88 years old, SD: 22.97 years old	
Time of Residence Mean	17.11 years old	

The malformations observed were: diaphragmatic hernia, congenital heart disease, myelomeningocele, and tuberous sclerosis. We registered a miscarriage rate in women between 15 and 45 years of age of 3.70% (4/109). A summary of clinical manifestations is presented in **Table 2**. As for cancer, in the last year (incidence), two cases were identified (one was breast cancer and the other one was skin cancer), with a gross rate of 394/100,000 residents. By prevalence, there are eight cases (four cases of skin cancer, two of breast cancer, one of bladder cancer, and one of B-cell lymphoma), with a gross rate of 1377.9/100,000. The average cancer mortality rate was 118/100,000, with three cases—one of leukemia in 2012, one of liver in 2013, and one of pancreas in 2014.)

Asthenia, as the presence of fatigue, depression and/or insomnia, was a manifestation spontaneously reported during the survey associated with one or more of the disorders mentioned above. Another spontaneously reported manifestation was the presence of rapidly growing tumor masses in the upper airways (laryngeal nodules, nasal polyps, and adenoid vegetation), creating respiratory obstructions requiring surgical treatment. This was reported by 7 young women and one man residing in the surroundings of the bioethanol plant.

As for the Pearson correlation analysis, the occupation variable had no significant relation with none of the pathologies but it significantly related children with acute respiratory disorders and asthma, elder people with dermatitis, conjunctivitis, headaches and digestive distress, and women with dermatitis, conjunctivitis, headaches and digestive distress. In a subgroup of 435 residents—from which we excluded tobacco and alcohol consumers (both substances being considered confusion factors)—we observed that 66% of the population had at least one of these conditions, 46% had two, and 26% had 3. Also, 63% of children had at least one. Children having two or more conditions are the most affected in all age groups.

Table 2. Health disorders in San Antonio and residential San Antonio neighborhoods potentially associated with environmental pollution.

Clinical Manifestations	Amount	Prevalence
Recurrent respiratory disorders, excluding asthma	182	36%
Bronchial asthma	85	17%
All respiratory disorders	267	53%
Pink eye—Conjunctivitis	158	31%
Headaches	135	27%
Dermatitis	116	23 %
Digestive Distress (dyspepsia)	112	22%
Cancer in the last 5 years	8	1.58%
Birth defects in the last 5 years	4	14.5%
Miscarriages by women aged 15 - 45	4	3.4%

4. Discussion

General Dimensions: **Airway** disorders have compromised over half of the residents, something that did not happen before the bioethanol plant started operating in 2012. The subgroup of people with **masses in upper airways** lives less than 100 meters away from the industrial plant, showing a very suggestive spatial association with the distillery (see Figure 2).

There was a large group of **asthmatic** neighbors, especially the epidemiological reference group (children aged 6 and 7) whose use of bronchodilator inhalers was confirmed in more than one every two children (57%) while, as stated by the Global Asthma Network, the burden of asthma (measured as people using bronchodilator inhalers) in Argentina is 14% [7] [8]. **Conjunctivitis** cases were widespread (one every three residents). No national reference figures are available, but the American Optometric Association reports a 1.3% prevalence, same as the UK [9] [10]. The conjunctivitis cases found show no seasonal variations, as would happen with allergic conjunctivitis (the commonest among general population). Conversely, a typical evolution of chemical conjunctivitis was observed that people affected themselves to associate with the air pollution generated by the bioethanol plant, as they report not having suffered from this condition before 2012. Also suggestive was the fact that this epidemic conjunctivitis outburst coexisted with a case of conjunctival squamous cell carcinoma in a male neighbor who had previously had pink eye syndrome. The presence of **persistent headache** which, according to the WHO [4], affects a variable percentage between 1.7% and 4% of the world population, affected a fourth of the neighbors in the case under study. Notably, the affected people reported that when they

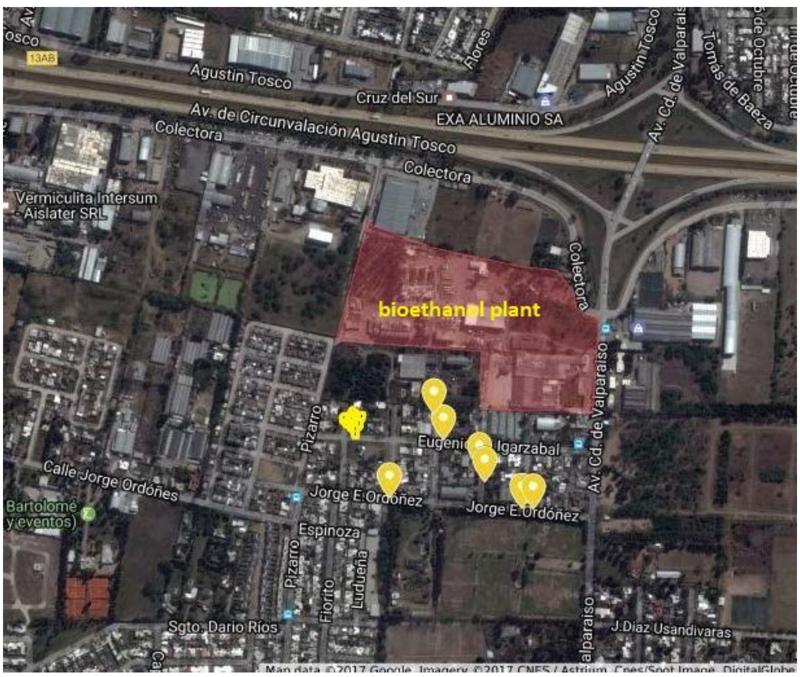


Figure 2. Spatial relation between households of neighbors featuring masses in upper airways and the bioethanol distillery.

leave the neighborhood, the headache goes away and it comes back when they return home. World reports on **allergic dermatitis** prevalence show figures ranging from 1% to 3% [11] [12] [13]. In the area under study, however, this condition was observed in 23% of the population. The highly prevalent irritant dermatitis and an increase in skin cancer cases (the most frequent location for cancer in this population) constitute an association suggesting continued, high exposure to skin-toxic substances. **Digestive distress** is a frequent manifestation difficult to quantify. However, 112 people out of the population under observation (22%) reported having persistent digestive distress, vomiting, stomach burning, nausea, and they had not suffered from these symptoms before perceiving the constant "smell" coming from the bioethanol plant.

The analysis of clinical manifestations allowed us to verify the convergence of medical conditions in the same people, thus being a syndromic pattern known as **Multiple Chemical Sensitivity Syndrome** (MCSS) [14] [15]. Consistent with this finding, the proportion of residents with distinctive clinical manifestations (dermatitis, respiratory disorders and asthma, pink eye syndrome, headaches, and digestive distress) associated with chronical decay, fatigue, depression and/or insomnia, are typical cases of MCSS, also found in children, who are probably the most affected. The criteria of the MCSS 1999 Consensus [14] set out that it is: 1) *a chronic condition*; 2) *with symptoms that recur reproducibly when there is chemical exposure*; 3) *in response to low levels of exposure*; 4) *to multiple unrelated chemicals*; 5) *improve or resolve when incitants are removed*; 6) *occur in multiple organ systems*. All of these conditions are present in the community living in the surrounding area of the bioethanol plant. They are more frequent in the elderly and in children, probably because they are the ones that stay most at home, subject to higher exposure. Ashford and Miller describe four MCSS affected groups, the fourth being formed by "*members of contaminated communities* [*of both genders and of all ages*] *exposed to air and water pollution from toxic waste dumps*, *aerial pesticide spraying*, *groundwater contamination*, *or other industrial exposures*." [16]. A variety of MCSS is the so-called "Sick Building Syndrome" described in 1997 [17] [18] and recognized by the WHO, where the symptoms manifest in people sharing a common environment, whether work-related or home-based. This nosological category seems to be the one that better fits the situation of the San Antonio neighbors, in this case giving rise to a "**Sick Neighborhood Syndrome**".

The incidence of **cancer** (393.7/100,000) turned out to be higher than that reported by the Provincial Tumor Registry (RPT, for its Spanish acronym) for the city of Córdoba in 2009 [19] (254.7/100,000), where the expected incidence (1.3 cases) was lower than that actually observed (2 cases)—which, considering previous background information and studies in the neighborhood, suggests a recent increase in these pathologies. The cancer prevalence rate (1378/100,000) was also higher than that reported by IARC in Cancer Today (793,5/100,000) [20]: 4.5 prevalent cases were expected but 8 cases were actually identified, showing a

marked increase in skin cancer cases (50%). However, our mortality results showed a lower rate than that informed by the RPT (118/100.000 and 135/100.000, respectively) [19]. This might indicate that, when the study was performed, the population under observation featured a low prior burden of cancer and, therefore, low current mortality (3 people have died of cancer in the past 5 years, while 3.4 cancer deaths were expected). Still, figures are very low and indeterminate biases may be operating.

As for **birth defects**, the rate in the past 5 years was 14.8%, with a 28.6% rate in the last year. These results are clearly at odds with those provided by the National Congenital Anomalies Registry of the Argentine Ministry of Health, which in 2012, reported a rate of 1.6% for the city of Córdoba [21]. The birth rate in the San Antonio neighborhood was similar to that of the rest of the city of Córdoba. However, the number of children born with malformations was exceedingly higher. Environmental chemical contamination can alter the normal gender distribution in the population, this effect we did not detect in our study.

All cases registered to relate to families residing a few meters away from a pollution source (bioethanol plant) whose products have been associated in other studies with birth defects and embryopathies [22] (see **Figure 3**). While the prevalence of miscarriages in San Antonio shows no significant differences from the rest of the country (3.67% and 3.00%, respectively) [23], the results obtained suggest there would be an extremely high risk of congenital anomalies for pregnant women who conceive their children and live throughout the pregnancy in this area of the city.

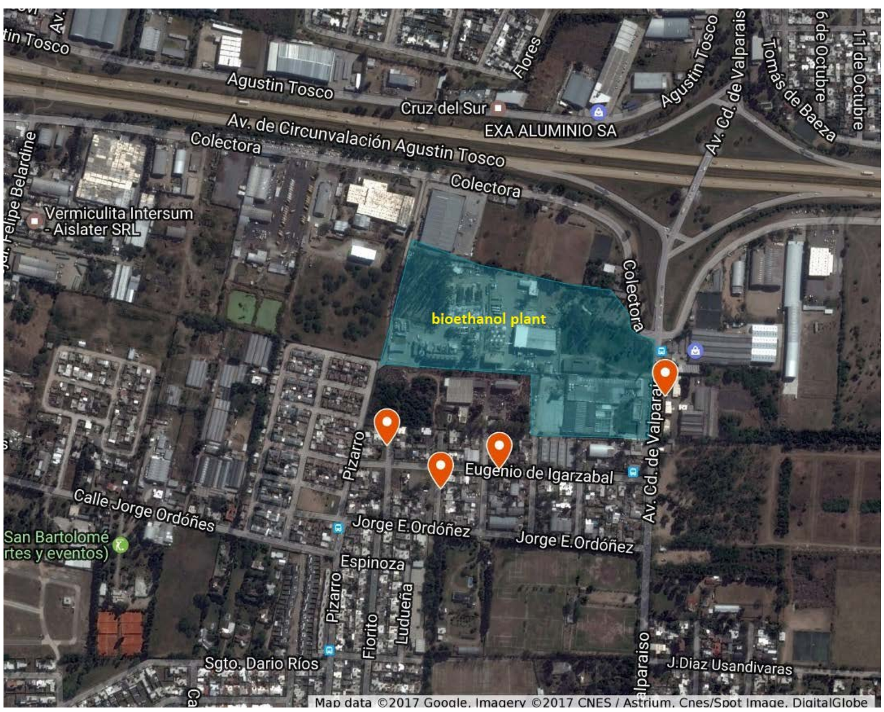


Figure 3. Location of houses of families that have children with malformations and their relation to the bioethanol plant.

Potential Environmental Pollutants of the San Antonio Neighborhood. Exposure to chemical substances from the bioethanol plant in San Antonio would explain the clinical features found in the area's population. These pollutants were identified in the environmental audit conducted by the company itself and were detected by court-ordered environmental expert studies. Aldehydes such as acetaldehyde and formaldehyde are the most toxic ones Aldehydes acetaldehyde and formaldehyde are the most toxic ones, as described in their WHO chemical safety cards [24] [25] and the main candidates for explaining this impact on health (also, hexane, acetic acid, as well as ethyl and methyl alcohol would be involved in the set of contaminants that seem to be acting on the neighborhood's environment) [26] [27] [28]. In 2014, provincial courts ordered two expert inspections of the discharge of the Porta Hnos. plant's fermenters and of the air in the streets of San Antonio. These inspections confirmed the presence of formaldehyde, toluene, and xylene. Toluene absorption works at the pulmonary level via inhalation in the form of gas. This substance behaves as a depressant of the Central Nervous System and exposure to vapors containing toluene produces irritation in the conjunctiva, the skin and the mucous membranes of airways. It also causes severe embryopathy when pregnant women inhale it, given its narcotic effects [29]. Xylene absorption also works at the pulmonary level via inhalation in the form of gas. It produces irritation in the conjunctiva, the skin and the mucous membranes of airways. Formaldehyde derives from methanol oxidation in the corn fermentation process. Its toxicity stems mainly from its highly irritant properties for living tissue that comes in contact with it. The commonest symptoms of exposure are irritation in the eyes, nose and throat, and dermatitis, both primary and by sensitization. High concentrations are toxic for cells and derive in degeneration and necrosis of the mucous and epithelial layers of tissue. Formaldehyde spread in the air is rapidly absorbed through the lungs. The WHO confirms there is enough evidence in humans to affirm that formaldehyde causes tumors in the rhinopharynx (a suggestive piece of data concerning the eight people in the area under study with tumor masses in their upper airways) and leukemia.

These chemical plants can also contaminate groundwater. In the case of this distillery, its toxic emissions are mainly gaseous, its liquid effluents are eliminated by the sewage system of the city of Córdoba and the symptoms of the affected population refer to air pollution.

The three gas chemical pollutants found in 2014 in the air of San Antonio provide biological plausibility to the symptoms suffered by the population affected, even without considering mixes and the other pollutants identified in the samples taken. Even these three toxic substances are described in scientific literature as triggering MCSS in shared environments [18] [30]. The fact that MCSS is caused by low-level, demonstrable exposures means that people other than those affected are capable of perceiving the presence of the substance through odor, even if no symptoms arise. The exposures causing the symptoms are many times below the standard deviation set in average guidelines of exposures that

are known to be capable of causing negative responses in people, although there is still no clear knowledge on the average concentrations triggering negative or unpleasant responses in most "normal" people.

As already stated in connection with the MCSS Consensus, it responds to low doses of different, unrelated chemical substances, preferably turning to environmental pollutants when explaining the concurrence of irritant symptoms for which there is no specific treatment. Those affected must avoid contact with the substances triggering the symptoms, as maintaining such contact will only favor the increase and seriousness of the clinical condition and the presence of new intolerances [14]. It is worthy of note that amongst those who presented two or three manifestations of this syndrome, children were the most affected of all groups under study.

By way of conclusion, the population assessed reports a high prevalence of asthma, conjunctivitis, headaches, and dermatitis, with most neighbors having clinical features compatible with MCSS. A concerning multiplication of people with vegetative masses in upper airways is also observed. Data on cancer and congenital anomalies also suggest a growing trend, although, given the small number of cases, these would be insufficient to make a statement in this regard. All of the above together make up a medical picture compatible with WHO's Sick Building Syndrome, in this case, forming an unprecedented Sick Neighborhood Syndrome—that is, a neighborhood where gas effluents were identified (formaldehyde, toluene, xylene and others) coming from an adjacent bioethanol distillery. Urgent measures ought to be considered to protect the collective health of the population living in this area.

The protection of the environmental health of this population requires eliminating from the ambient air the contamination generated by the bioethanol distillery, this, perhaps, could be achieved with filters that trap toxic gases. Or moving the distillery to an uninhabited region, there is no record of the existence of an industrial plant of this type in a fully inhabited place.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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